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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,034	08/24/2000	Daniel F. Klessig	RUT 98-0073	8125

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EXAMINER
MEHTA, ASHWIN D

ART UNIT	PAPER NUMBER
1638	8

DATE MAILED: 10/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/623,034	KLESSIG ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7,10-13,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,7,10-13, 15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The objection to the oath/declaration is withdrawn, in light of the newly submitted oath/declaration.

3. The objections to the specification for failure to comply with 37 CFR 1.821-1.825 and for not referring to the multiple parts of Figures 1-4 and 6-8 are withdrawn, in light of the amendments.

4. The objection to claims 14-17 is withdrawn, in light of their amendment or cancellation.

5. The rejection of claims 1-17 under 35 U.S.C. 112, 1st paragraph, under item 8 of the Office action mailed 15 January 2002 is withdrawn and replaced with the enablement rejection below.

6. The rejection of claims 1-17 under 35 U.S.C. 102(b) is withdrawn, in light of the claim amendments.

7. The rejection of claims 1-17 under 35 U.S.C. 103(a) is withdrawn in light of the claim amendments.

Claim Objections

8. Claims 1, 7, 10, and 11 are objected to for the following reasons:

In line 4 of claim 1 and line 16 of claim 10, the word "cyrptogein" is misspelled.

In claim 7, it is suggested that the recitation "which" be replaced with --wherein said transgenic plant--.

Claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form.

Claim 11 attempts to limit the method of claim 10 by requiring the WIPK enzyme to be produced constitutively. However, parent claim 10 indicates that the nucleic acid molecule encoding the WIPK enzyme is operatively linked to the figwort mosaic virus (FMV) 35S promoter. If Applicants are referring to the FMV 34S promoter (see below), this promoter is constitutive, and the method of claim 10 could only produce the enzyme constitutively. The limitation of claim 11 then does not further limit the scope of claim 10.

Claim Rejections - 35 USC § 112

9. Claims 1, 4, 5, 7, 10-13, 15 and 16 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record stated in the Office

action mailed 15 January 2002 under item 6. Applicants traverse the rejection in the paper received 06 June 2002. Applicants' arguments have been fully considered but were not found persuasive for the issue regarding the definiteness of the term "WIPK."

Applicants have amended claims 1 and 10 by indicating that the transgenic plant is stably transformed with construct comprising a molecule selected from the group consisting of GenBank Accession No. D61377 or a sequence having 90% sequence identity therewith encoding a WIPK enzyme. Applicants argue that the prior art reference, Seo et al., is referred to throughout the specification and is incorporated by reference (response, page 10, 2nd full paragraph).

However, the claims still recite the term "WIPK." As discussed in the last Office action, there is confusion in the art as to whether this protein should be referred to by this acronym, as it stands for "wound-induced protein kinase," since the enzyme taught Sao et al. is not wound-induced, or involved in the wound response. Confusion therefore remains if any nucleic acid sequence, including those referred to in the claims as having 90% sequence identity with GenBank Accession No. D61377, is said to encode a WIPK enzyme.

Further, GenBank Accession No. D61377 indicates that the sequence has been revised since the publication of the Sao et al. article. It is suggested that the sequence taught by Sao et al. be submitted as part of the sequence listing (see below), and claims 1 and 10 be amended to refer to this sequence by its assigned sequence identifier. It is also suggested that the recitation "a functional WIPK enzyme" be replaced with --an amino acid sequence that has the activity of the amino acid sequence encoded by SEQ ID NO:___ of conferring disease resistance--. In claim 4, it is suggested that the recitation "DNA construct comprises a WIPK-encoding region"

be replaced with --nucleic acid molecule is-- (however, see the indefinite rejection of claim 4 below). For claims 11 and 12, it is suggested that the recitation "produces a WIPK enzyme" be replaced with --expresses said nucleic acid molecule-- (however, see the indefinite rejections of claims 4, 5, and 12 below). For claim 13, it is suggested that the recitation "DNA construct comprises a tobacco WIPK coding sequence" be replaced with --nucleic acid molecule is from tobacco--.

In claim 4: the claim recites the limitation "the DNA construct" in line 2. There is insufficient antecedent basis for this limitation in the claim or in parent claim 1.

In claims 4, 5, and 12: the claims are indefinite because they broaden the scope of their parent claims. Claims 1 and 10 require the nucleic acid molecule to be operatively linked to the FMV 35S promoter. If Applicants are referring to the FMV 34S promoter (see below), this promoter is constitutive. However, claims 4, 5, and 12 require the enzyme to be produced inducibly, which requires a different promoter.

10. Claims 1, 4, 5, 7, 10-13, 15, and 16 remain rejected under 35 U.S.C. 112, first paragraph, is containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record stated in the Office action mailed 15 January 2002 under item 7. Applicants traverse the rejection in the paper received 06 June 2002. Applicants' arguments have been fully considered but were not found persuasive.

It is noted that Applicants have addressed the written description and enablement rejections together. Applicants are notified that these are two separate rejections that should also be addressed separately. However, in the interest of compact prosecution, and as the remaining written description and enablement issues are similar, Applicants arguments shall be considered.

Applicants argue that claim 1 has been amended to call for a DNA construct comprising the nucleic acid sequence set forth in GenBank Accession No. D61377 or a sequence that is 90% identical to it and encodes an enzyme having WIPK function (response, page 12, 2nd full paragraph). However, it is noted that the sequence in this GenBank entry has been revised since the filing of the instant application, and can be revised again in the future. It is suggested that the version of the sequence in GenBank Accession No. D61377 as it appeared on the priority date of the instant application be submitted as part of the sequence listing, and that the claims refer to the assigned sequence identifier. Along with the sequence, Applicants should also submit evidence that proves that this was the sequence of the GenBank entry as of the priority date of the instant application.

11. Claims 1, 4, 5, 7, 10-13, 15, and 16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn towards any transgenic plant expressing an N gene and having enhanced resistance to a plant-disease causing agent selected from the group consisting of tobamoviruses, elicitin-producing fungi, parasiticein-producing fungi, cryptogein-producing

fungi, harpin-producing bacteria, tobacco mosaic virus, and Phytophthora fungi, wherein said transgenic plant is stably transformed with a nucleic acid construct comprising the FMV 35S promoter operatively linked to a nucleic acid molecule selected from the group consisting of a sequence set forth in GenBank Accession No. D61377 or any sequence having 90% sequence identity therewith encoding any functional WIPK enzyme; or a method of making said transgenic plant.

The specification teaches that a 44 kD tobacco protein designated WIPK is induced in TMV-infected tobacco plants, and that kinase activity of the protein is also activated (page31, line 1 to page 34, line 27). The specification teaches that activation of this WIPK in the TMV infected plants is also dependent on the presence of the N resistance gene, is not dependent on salicylic acid, and is associated with systemic acquired resistance (SAR; page 34, lines 7-34). The specification also indicates that transgenic plants constitutively expressing WIPK, taught by Seo et al., had elevated levels of salicylic acid and pathogenesis-related proteins following wounding (page 37, lines 21-27). The specification also teaches that WIPK is activated by treatment with fungal elicitins derived from Phytophthora (page 38, lines 21-24), harpin, a bacterial-encoded elicitor, and to the fungal elicitins parasiticein and cryptogein (page 15, lines 9-13).

However, the specification does not teach WIPK coding sequences that can be used to make the claimed plants other than that taught by Seo et al. As discussed above, the specification teaches that a 48 kD protein, rather than the WIPK taught by Seo et al., encodes a tobacco wound-activated kinase. The specification teaches that a WIPK-specific antibody, produced using a peptide from the N-terminus of the protein taught by Seo et al., bound a 44 kD

peptide (reported as 46 kD by Seo et al.), and that while mRNA encoding this peptide was transiently induced upon wounding, the encoded protein was not (page 31, line 1 to page 32, line 27; page 35, lines 3-26). The specification teaches that WIPK- and SIPK- (salicylic acid-induced kinase) specific antibodies were used to determine that a 48 kD tobacco SIPK, and not the 44 kD WIPK encoded by the cDNA taught by Seo et al., is the wounding-activated kinase (page 36, lines 13-24). It is therefore unpredictable that transgenic plants transformed with coding sequences for other proteins designated WIPK, which encode wound-activated kinases, would have enhanced resistance to disease-causing agents. Further, Zhang et al. (Proc. Natl. Acad. Sci., USA, 1998, Vol. 95, pages 7225-7230) call into question the designation of WIPK orthologs as wounding-activated kinases, and stress that further analysis is needed to firmly establish the relationship between these genes and the activated kinases (page 7229). In light of this confusion over the designation "WIPK", it is unpredictable what coding sequences are encompassed by the claims. It would require undue experimentation by one skilled in the art to determine whether not WIPK homologs known in the art are wound-activated kinases. Such kinases would not be encompassed by the claims, since the exemplified kinase of the invention, taught by Seo et al., is apparently not wound-activated, despite its name. The specification does not provide sufficient guidance for one to identify WIPKs that can be used with the invention, from those that cannot.

In the paper received 06 June 2002, Applicants argue that the claims have been amended to call for a DNA construct comprising the nucleic acid sequence set forth in GenBank Accession No. D61377 or a sequence that is 90% identical to it and encodes an enzyme having WIPK function (response, page 12, 2nd full paragraph). However, as discussed above, sequences

that appear in GenBank and other databases can be changed at any time. The claims cannot rely on sequences that were unknown at the time the invention was filed. See the suggestions above.

The specification does not teach that transgenic plants overexpressing WIPK actually conferred resistance against any pathogen. While the specification indicates that Seo et al. teach that transgenic plants constitutively expressing WIPK had elevated levels of salicylic acid and pathogenesis-related proteins following wounding, it does not teach that the transgenic plants enhanced any disease resistance against any plant-disease causing agent. While the specification also indicates that the 44 kD tobacco WIPK is induced and activated in non-transgenic, TMV-infected tobacco plants containing the N gene, and that the tobacco WIPK is activated by treatment with fungal elicitins derived from Phytophthora, harpin, parasiticein, and cyrptogein, it does not teach that transgenic plants overexpressing WIPK having enhanced resistance of the plant against any plant-disease causing agents were produced. Zhang et al. (Plant Cell, 2001, Vol. 13, pages 1877-1889) teach transgenic plants in which the tobacco WIPK coding sequence was under the control of an inducible promoter. Expression of WIPK did not lead to an increase in activity, despite an increased production of the WIPK protein (page 1880). Zhang et al. also teach that transgenic plants constitutively expressing WIPK did not show higher WIPK activity, even though the protein was overexpressed. Zhang et al. also refer to another report in which WIPK overexpression led to increase an in WIPK activity. However, these differing results could not be explained (page 1885). In light of these teachings, undue experimentation would be required by one skilled in the art to make transgenic plants overexpressing WIPK in an active form and which confers enhanced resistance to the disease-causing agents listed in the claims. Given the breadth of the claims, unpredictability of the art and lack of guidance of the

specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 103

12. Claims 1, 4, 5, 7, 10-13, 15, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seo et al. (Science, 1995, Vol. 270, pages 1988-1992) in view of Sanger et al. (Plant Mol. Biol., 1990, Vol. 14, pages 433-443), Gatz et al. (Mol. Gen. Genet., 1991, Vol. 227, pages 229-237), Enyedi et al. (Proc. Natl. Acad. Sci., USA, 1992, Vol. 89, pages 2480-2484), Yu et al. (Proc. Natl. Acad. Sci., USA, 1995, Vol. 92, pages 4088-4094), and He et al. (MPMI, 1994, Vol. 7, pages 289-292),

The claims are broadly drawn towards any transgenic plant expressing an N gene and having enhanced resistance to a plant-disease causing agent selected from the group consisting of tobamoviruses, elicitin-producing fungi, parasiticein-producing fungi, cryptogein-producing fungi, harpin-producing bacteria, tobacco mosaic virus, and Phytophthora fungi, wherein said transgenic plant is stably transformed with a nucleic acid construct comprising the FMV 35S promoter operatively linked to a nucleic acid molecule selected from the group consisting of a sequence set forth in GenBank Accession No. D61377 or any sequence having 90% sequence identity therewith encoding any functional WIPK enzyme; or a method of making said transgenic plant.

Seo et al. teach transgenic plants, homozygous for the N gene, produced by transforming plants with the nucleotide sequence deposited with GenBank under accession number D61377,

encoding a WIPK enzyme. The expression of salicylic acid and pathogenesis-related (PR) genes was increased in the transgenic plants (pages 1989-1991).

Seo et al. do not teach the FMV 35S promoter or an inducible promoter.

Sanger et al. teach the FMV 34S promoter, that its activity approximates that of the CaMV 35S promoter, and assert that it broadens the options in higher plant expression vector design, due to the significant variation in promoter/enhance region sequences between the FMV34S and CaMV 35S promoters (pages 437-439, 441).

Gatz et al. teach a Tn10-encoded tet repressor-operator system to regulate expression of an engineered CaMV 35S promoter in transgenic tobacco plants. Maximal induction of the promoter is achieved after 30 min. upon application of 0.1 mg/l tetracycline. Gatz et al. teach that the tet system is fast, efficient, and can be used for the regulation of integrated genes and for specifically inducing expression of transferred genes at different stages of plant development (abstract, pages 231-234, 236).

Enyedi et al. teach that increasing SA, followed by an increase in PR proteins, in NN-genotype plants increased the plant's resistance to infection by tobacco mosaic virus (TMV) pages 2480-2484).

Yu et al. teach that elicitins, including cryptogein and parasiticein, which are produced by species of the genus Phytophthora, cause a hypersensitive response (HR) and induce systemic required resistance (SAR) in plants (pages 4088-4091).

He et al. teach that the HR response is triggered in response to bacteria that produce harpin (pages 289-291).

It would have been obvious and within the scope of one of ordinary skill in the art at the time the invention was made replace the promoter that was operably linked to the WIPK-encoding nucleotide sequence of Seo et al. with any other desired promoter, including the FMV 34S promoter of Sanger et al. or the tetracycline repressor-operator system of Gatz et al. A wide variety of promoters are available in the art, which researchers routinely use to achieve a desired end. One would have been motivated to use the FMV 34S promoter, given its activity approximates that of the CaMV 35S promoter, as taught by Sanger et al. Alternatively, one would have been motivated to use the an inducible, such as the tetracycline repressor/operator controlled promoter, given the speed, efficiency, and control it offers in controlling transgene expression, as taught by Gatz et al. As the transgenic plants taught by Seo et al. have increased expression of SA and PR-related genes, it would have been obvious that the transgenic plants had enhanced disease resistance against TMV, elicitin-producing fungi, including Phytophthora, and harpin-producing bacteria, given that it was known that plants induce an HR response as part of their defense against diseases caused by these pathogens, as taught by Enyedi et al., Yu et al., and He et al.

In the paper submitted 06 June 2002, Applicants argue that there is no motivation or suggestion in Seo et al. to modify the promoter used to express the WIPK-encoding DNA construct. Applicants stress the Gatz et al. was published four years prior to Seo et al., and that if the modification was obvious, the means to do so was available to Seo et al.

Applicants' arguments were fully considered but were not found persuasive. A reference need not actually suggest changes or possible improvements that can be made (*In re Sheckler*, 438 f.2d 999, 1001; 168 USPQ 716, 717 (CCPA 1971)), and the Examiner can rely on a

conclusion of obviousness from knowledge that is common knowledge or common sense to one of ordinary skill in the art without any specific hint or suggestion in a particular reference. See *In re Bozek*, 416, F.2d 1385, 1390, 163 USPQ 545, 549 (CCPA 1969).

Applicants also argue that hindsight reconstruction was used to combine the references (response, page 14, 1st full paragraph and the paragraph bridging pages 14-15). However, if the judgment of obviousness takes into account only knowledge that was within the level of ordinary skill in the art at the time of the invention and does not include knowledge gleaned only from the applicant's disclosure, the combination of the references is proper. See *In re McLaughlin*, 443, F.2d 1392, 1395, 170 USPQ 209, 212 (CCPA 1971). As pointed out by the Applicants, the promoter system of Gatz et al. was known in the art, and reasons to use it are asserted by Gatz et al. Reasons for using the FMV 34S promoter are also asserted by Sanger et al., as discussed above.

Summary

13. Claims 1, 4, 5, 7, 10-13, 15, and 16 remain rejected.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this

application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

A.M.
October 7, 2002

ASHWIN D. MEHTA, PH.D
PATENT EXAMINER